INDO AMERICAN JOURNAL OF PHARMACEUTICAL RESEARCH

# A RETROSPECTIVE STUDY ON PRESCRIBING PATTERN OF DRUGS IN FEMALE INFERTILITY AT A TERTIARY CARE CENTRE IN SOUTH INDIA

**Dr Shaheda Siddiqui[1*], Dr Fatima Tahniyath[1], (Dr) Ayesha Butool[1], (Dr) Kauser Fatima[1], Dr Raga Reddy[2], Dr Roya Rozati[2]**

[1]*Dept of Pharmacy Practice, Deccan School of Pharmacy,Hyderabad.*
[2]*Dept of OBGYN, Deccan College of Medical Sciences, Owaisi Hospital and Research Centre, Hyderabad.*

**ARTICLE INFO**

**Article history**
Received 15/03/2017
Available online
31/03/2017

**Keywords**
Infertility,
Retrospective,
Prescriptions,
Pregnancy,
Rational Drug Use.

**ABSTRACT**

Introduction: A disease of the reproductive system defined by the failure to achieve a clinical pregnancy after12 months or more of regular unprotected sexual intercourse. The demand for overcoming infertility is increasing year by year. Hence there is a quantum jump in the technology used in the diagnosis and therapy of infertility. Aim/ Objective: To observe the rationality among the prescriptions with principle aim to study the efficacy, tolerability, safety and cost-effectiveness of the drugs used in infertility cases and to evaluate the prescribing pattern and criteria for selection of drugs for infertility. Methodology: A retrospective, observational study was conducted in the department of Obstetrics and Gynecology at Owaisi Hospital and Research Centre, Hyderabad, India. The duration of the study was 15 month period from September 2015 to Dec 2016 on 300 consenting female infertility patients. Results: In our study 43% of patients belonged to age group 26-30. 45% were newly diagnosed patients,65.3 % of patients had primary infertility and whereas 34.6% had secondary infertility. Menstrual irregularity were the most common cause of infertility (36%). The patients were treated with drug alone depending on their age and cause of infertility. Clomiphene Citrate (12.76%) was the most common drug prescribed for ovulation induction.55.3 % of patients conceived during our study, women who failed to achieve pregnancy needed Assisted Reproductive Technology. The PDD and DDD was calculated to achieve rationality of prescriptions. Conclusion: Infertility is a critical component of reproductive health which is a global public health challenge. The use of pharmacoepidemological data can help in designing, delivering and evaluating many interventions to improve the use of fertility drugs and outcome of patients as Infertility is a global health issue.

***Corresponding author***
**Shaheda Siddiqui**
Assistant Professor
Deccan School of Pharmacy
Dar us Salam, Hyderabad.
9948219786
shaheda.pharmd@gmail.com

*Please cite this article in press as **Shaheda Siddiqui** et al. A Retrospective Study on Prescribing Pattern of Drugs in Female Infertility at A Tertiary Care Centre in South India. Indo American Journal of Pharmaceutical Research.2017:7(03).*

## INTRODUCTION

The ability to reproduce and to perpetuate the species is one of the most remarkable features of the living organisms. Fertility and infertility have been a major concern to mankind since time immemorial. Infertility is seldom, if ever, a physically debilitating disease. It may, however, severely affect the couple's psychological harmony, married life and also the healthcare services along with the social environment [1].The clinical definition of infertility used by the World Health Organization (WHO) is "a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after12 months or more of regular unprotected sexual intercourse"[2]. Infertility can be subdivided into primary infertility, that is, no prior pregnancies, and secondary infertility, referring to infertility following at least one prior conception [3].Globally, most infertile couples suffer from primary infertility [4]. The demand for overcoming infertility is increasing year by year. Hence there is a quantum jump in the technology used in the diagnosis and therapy of infertility. There is also a tremendous escalation of cost in management of infertility cases. This fact is an important cause of concern in the economic development of a country. Therefore the following study is an attempt made to see the rationality among the prescriptions with principle aim to study the efficacy, tolerability, safety and cost-effectiveness of the drugs used in infertility cases and to evaluate the prescribing pattern and criteria for selection of drugs for infertility.

## MATERIALS AND METHODS

This Retrospective, observational study was conducted in the department of Obstetrics and Gynecology at Owaisi Hospital and Research Centre,Hyderabad, India. The duration of the study was 15 month period from September 2015 to Dec 2016 on 300 consenting female infertility patients. No Institutional ethics committee approval was required as it is a retrospective observational study and written informed consent was obtained from each patient before enrolment. Demographic details, necessary clinical data, and medication details were collected in a specially designed proforma. Data on utilization of different classes as well as individual drugs were subjected to descriptive analysis.

### Inclusion criteria:

Female patients presenting with infertility in the outpatient department of the hospital within the reproductive age group (20-40 years) consenting for the study.

### Exclusion criteria:

1. Cancer patients, at terminal stage.
2. Females before and after reproductive age.

### The data analysis was done as follows

1. Assessment of prescription pattern as per WHO drug use indicator.
2. The prescribed drugs were classified according to the Anatomical Therapeutic classification (ATC)-Defined Daily Dose (DDD) Classification.[5]
3. The prescribed Daily Dose (PDD) was calculated by taking the average of the daily doses of psychotropic drugs as PDD. The PDD to DDD Ratio was then calculated.[5]

## RESULTS

**Table 1 Based on Age.**

| Age | No. of Patients (%) |
|---|---|
| 20-25 | 122(40.6) |
| 26-30 | 129(43) |
| 31-35 | 33(11) |
| 36-40 | 16(5.3) |

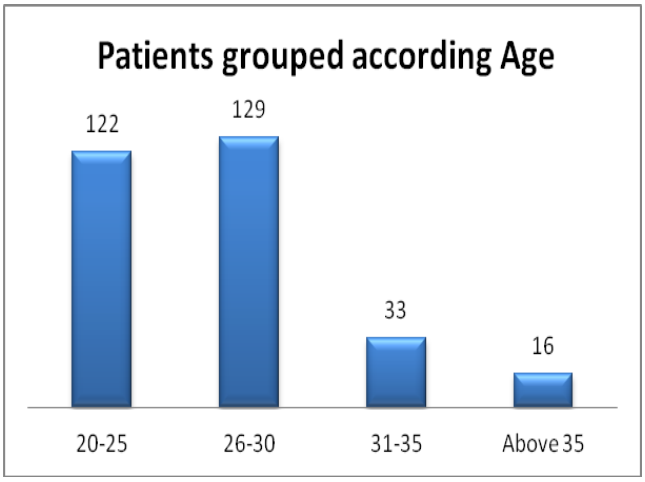


**Figure 1: Based on Age.**

**Table 2 Grade of Infertility.**

| Grade of Infertility | No. of Patients (%) |
|---|---|
| Primary | 196(65.3) |
| Secondary | 104(34.6) |

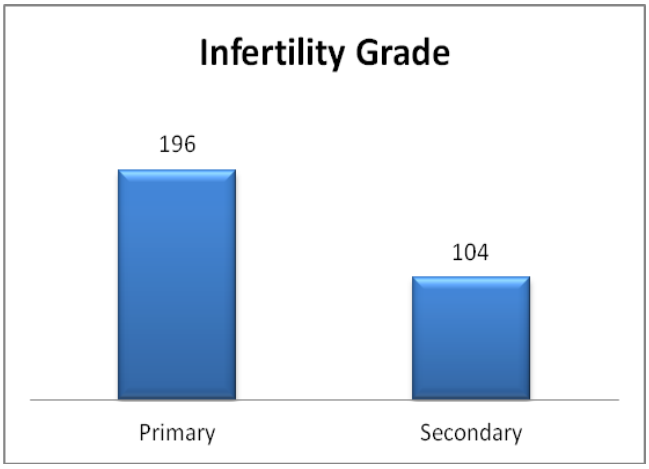


**Fig 2: Grade of Infertility.**

**Table 3 Based on Associated Co- morbid Conditions/ Cause of Infertility.**

| Cause of Infertility | No. of Patients (%) |
|---|---|
| Polycystic Ovaries | 31(10.3) |
| Polycystic Ovarian Syndrome | 47(15.66) |
| Subclinical Hypothyroidsm | 16(5.3) |
| Endometriosis | 14(4.6) |
| Age related Ovulatory dysfunction | 12(4) |
| Hostile Mucus | 7(2.3) |
| Increase level of Prolactin | 24(8) |
| Menstrual irregularities | 108(36) |
| Genital Kochs | 14(4.6) |
| Unexplained | 27(9) |

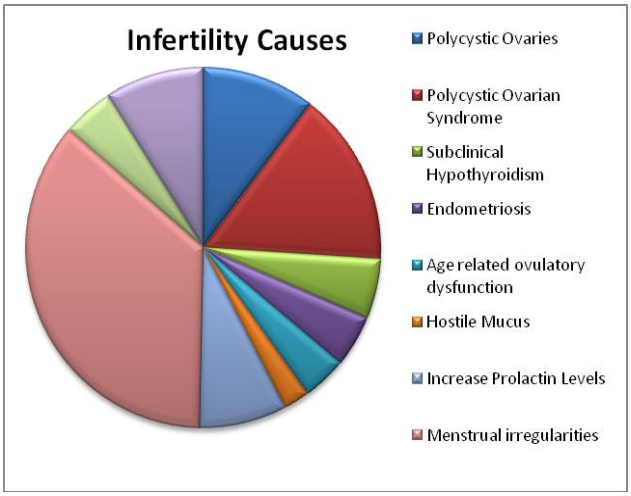


**Fig 3: Based on Associated Co- morbid Conditions/ Cause of Infertility.**

**Table 4. Distribution of Drugs prescribed in patients (N=300).**

| Name of the Drugs | % of Prescribed drugs |
|---|---|
| Siphene (Clomiphene Citrate) | 12.76 |
| Duphaston (Dydrogesterone) | 12.56 |
| Progynova(Estradiol Valerate) | 16.27 |
| Regesterone (Norethindrone acetate) | 8.70 |
| HCG (Human Chorionic Gonadotropin) | 1.18 |
| Positive(Pioglitazone) | 4.49 |
| Glyciphage(Metformin) | 2.03 |
| Tamoxifen(Tamoxifen Citrate) | 3.89 |
| Geocyst (Metformin+Myoinositol) | 0.92 |
| Cabergoline(Cabergoline) | 0.35 |
| Folvite(Folic Acid) | 86.9 |
| Oflox(Ofloxacin) | 5.7 |
| Clindamycin(Clindamycin) | 0.46 |
| Norflox(Norfloxacin) | 0.79 |
| Anti Tubercular | 0.18 |
| Taxim (Cefixime) | 0.31 |
| Azwin(Azithromycin) | 0.26 |
| Monocef (Cefpodoxime) | 0.56 |
| Metrogyl IV(Metronidazole) | 0.05 |
| Augpen (Amoxycillin+ Potassium Clavunate) | 0.27 |
| Diclomol(Diclofenac+ Paracetamol) | 4.24 |
| Chymoral Forte(Chymotrypsin+Trypsin) | 0.39 |
| Voveran(Diclofenac Sodium) | 1.91 |
| Pyridoxine | 7.42 |
| Eltroxin(Levothyroxine) | 0.21 |
| Ebexid | 0.13 |
| Hydrocort(Hydrocortisone) | 0.10 |
| Zofer(Ondansetron) | 0.36 |
| Rabion(Rabeprazole) | 4.49 |
| Pantop(Pantoprazole) | 1.69 |

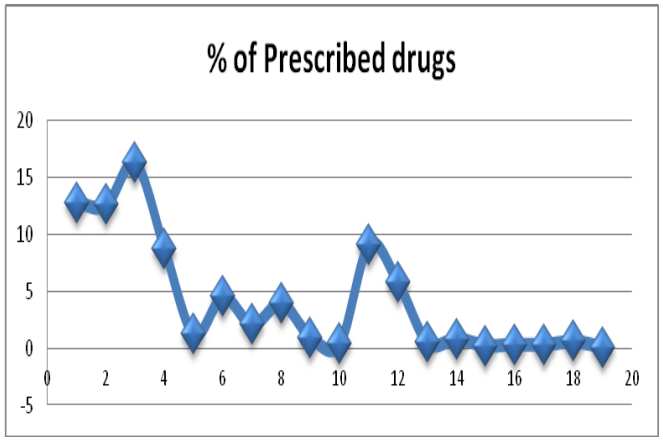


**Figure 4. Distribution of Drugs prescribed in patients (N=300).**

**Table 5: Distribution of Patients according to outcome of therapy.**

| Outcome of Therapy | No. of Patients (%) |
|---|---|
| Conceived | 166(55.3) |
| Not conceived | 73(24.3) |
| Missed Abortions | 12(4) |
| Ectopic Pregnancy | 4(1.33) |
| Left Against Medical Advice | 45(15) |

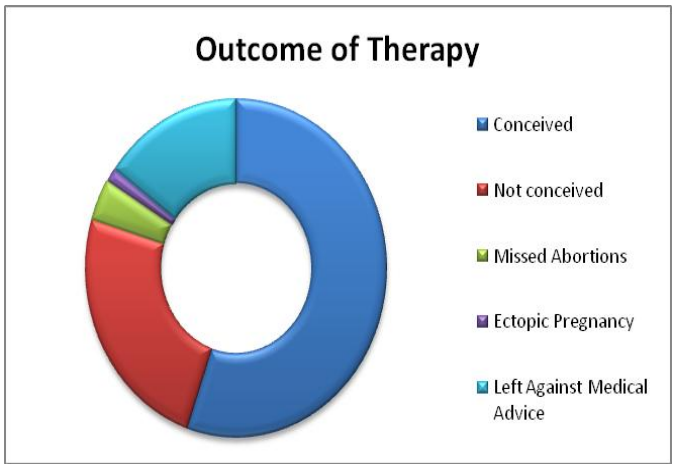


**Figure 5: Distribution of Patients according to outcome of therapy.**

**Table 6: WHO Drug Used Indicators:**

| Prescribing Indicators | Data |
|---|---|
| Availability of copy of Essential Drug list & Hospital Formulary | Yes |
| Total no. of Drugs in 300 Patients during the study period | 7569 |
| Average no. of drugs per patient during the study period | 25 |
| Total no. of Ovulatory Drugs in 300 Patients during the study period | 5328 |
| Percentage of Ovulatory drugs per patient during the study period | 70.3% |
| Percentage of Other drugs per patient during the study period | 21% |
| Percentage of Drugs prescribed by generic Name | 58% |
| Percentage of Prescriptions with an antibiotic prescribed | 8.62% |
| Percentage of Prescriptions with an Injection Prescribed | 1.34% |
| Percentage of Drugs prescribed from Essential Drug List / Hospital Formulary | 80% |

**Table 7: PDD Values & PDD/DDD Ratios of Ovulation Drugs prescribed in a sample of 300 Patients attending Infertility Unit.**

| DRUG | ATC CODE | ROA | DDD (mg) | PDD (mg) | PDD/DDD |
|---|---|---|---|---|---|
| Siphene | G03GB02 | Oral | 50 | 161 | 3.22 |
| Duphaston | G03DB01 | Oral | 10 | 31.7 | 3.17 |
| Progynova | G03DC02 | Oral | 2 | 8.2 | 4.10 |
| Regesterone | G03DC02 | Oral | 5 | 10.983 | 2.19 |
| Cabergoline | G02CB03 | Oral | 0.5 | 0.045 | 0.09 |
| Glyciphage | A10BA02 | Oral | 250 | 128.33 | 0.513 |
| Positive | A10BG03 | Oral | 15 | 17 | 1.13 |
| Tamoxifen | L02BA02 | Oral | 20 | 19.66 | 0.98 |
| Geocyst | A10BA02 | Oral | 500 | 116 | 0.23 |
| HCG-5000IU | G03GA01 | IM | 500 | 150 | 0.3 |
| Folvite | B03BB01 | Oral | 5 | 9.06 | 1.81 |

$$\text{PDD} = \frac{\text{Quantity of drug dispensed} \times \text{Strength of drug}}{\text{No. of Patients}}$$

**Table 8: DDD Values of Ovulation Drugs prescribed in a sample of 300 Patients attending Infertility Unit.**

| Drugs | No. of Prescribed Doses | Strength | DDD | WHO-DDD | DDD/300 Patients | | PDD |
|---|---|---|---|---|---|---|---|
| | | mg | mg | gm | mg | gm | |
| Siphene | 966 | 50 | 50 | 0.05 | 0.166 | 0.0016 | 161 |
| Duphaston | 951 | 10 | 10 | 0.01 | 0.03 | 0.000033 | 31.7 |
| Progynova | 1232 | 2 | 2 | 0.002 | 0.007 | 0.0000066 | 8.21 |
| Regesterone | 659 | 5 | 5 | 0.005 | 0.016 | 0.000016 | 10.98 |
| Cabergoline | 27 | 0.5 | 0.5 | 0.0005 | 0.0016 | 0.0000016 | 0.045 |
| Glyciphage | 154 | 250 | 250 | 0.25 | 0.83 | 0.000833 | 128 |
| Positive | 340 | 15 | 15 | 0.015 | 0.05 | 0.00005 | 17 |
| Tamoxifen | 295 | 20 | 20 | 0.02 | 0.06 | 0.00006 | 19.66 |
| Geocyst | 70 | 500 | 500 | 0.5 | 1.66 | 0.001666 | 116.6 |
| HCG-5000IU | 90 | 500 | 500 | 0.5 | 1.66 | 0.0016 | 150 |
| Folvite | 544 | 5 | 5 | 0.005 | 0.0166 | 0.000016 | 9.06 |

## DISCUSSION

In our study of 300 patients, 43% belonged to age group of 26-30 as shown in Table and Figure 1. 45% were newly diagnosed patients. 65.3% had primary infertility as depicted in Table and Figure 2. Causes of infertility are shown in Table and Figure 3 where menstrual irregularities (36%) were noticed as a common cause for infertility. Sub clinical hypothyroidism was observed in 5.3% of patients. Hashimoto's thyroiditis is the most common endocrinopathy in premenopausal women, and is associated with various gynecological problems, including recurrent miscarriages and unexplained infertility.Strict thyroid hormone supplementation egimen was followed to achieve desirable TSH levels.[6] The distribution of drugs prescribed in 300 patients during study period are depicted in Table and Figure 4 among which Clomiphene Citrate (12.76%) was commonly prescribed as ovulation induction drug as it has antiestrogenic action,which induces gonadotropin secretion by blocking estrogenic action,which induces gonadotropin secretion by blocking estrogenic feedback inhibition of pituitary[7]along with supportive therapy with Progynova (16.27%) as a study conducted by Gleicher et al have demonstrated the combined effet of estradiol and progesterone substitution of the luteal phase of ovulation induction cycles increases the overall pregnancy rate,especially in women beow 38 years of age and nulliparous women[8],progesterone supplementations were advised in patients as it is essential for luteal phase support in patients with luteal phase defect.[9] and Folic Acid supplementation (86.9%) as it is a well-established fact that folic acid supplementation reduces neural tube defects of fetus.[9] In patients with PCOS showing Clomiphene resistance,metformin was prescribed followed by regular menstrual cycles, reduction in hyperandrogenism and improvement in raes of ovulation and conception.[10]

The outcome of therapy is depicted in Table and Figure 5, Conceived were 166(55.3%) patients. As illustrated in Table 6, Total drugs prescribed in 300 patients during the study period of 15 months were 7569 among which ovulatory drugs were found to be 5328. Percentage of ovulatory drugs per patient contributed to 70.3% whereas other drugs advised were 21%. Average no.of drugs per patient were 25; drugs prescribed with generics were 58%. Antibiotics prescribed were 8.62%, Drugs from EDL and Hospital Formulary were 80%.

PDD-Prescribed Daily Dose of drugs and DDD- Defined Daily Dose was calculated as depicted in Table 7. The ratio of PDD/DDD was calculated for each drug and the prescribing pattern of drugs was found to be rational as well explained in Table 8.
In today's modern world, medical science has various new and advanced technologies like ART (Assisted Reproductive Technology) and IVF (In Vitro Fertilization) to help those numerous childless couples, who are seeking treatment of infertility, some tests should be initiated to provide the outcome prognosis for assisted reproductive technology [6]In the present study, the pattern of drugs used to treat infertility has been studied along with the evaluation of outcome of therapy in 300 patients after fulfilling the inclusion criteria.

## LIMITATIONS OF THE STUDY:

1. The sample size of the patients was small to calculate prescribing pattern of drugs in infertility cases.
2. Follow up duration is short.
3. Further studies in various hospitals are required which will broaden the knowledge about the management of infertility.

## CONCLUSION

Women with reproductive dysfunction who fail to achieve pregnancy need ART/IVF. The use of pharmacoepidemological data can help in designing, delivering and evaluating many interventions to improve the use of fertility drugs and outcome of patients as Infertility is a global health issue.

## CONFLICTS OF INTEREST:

No conflicts of interest to declare.

## ACKNOWLEDGEMENT

We would like to acknowledge Dr Roya Rozati, Prof HOD Department of Obstetrics and Gynecology, Owaisi Hospital and Research Centre and the team of experts of the department for their constant support and guidance during the study period.

**REFERENCES**


1. Sciarra J.Infertility : An International Health Problem. Int J Gynaecol Obstet.1994:46:156-163.
2. Zegers-Hochschild F,Adamson GD,de Mouzon J.et al. The International Committee for monitoring assisted reproductive technology(ICMART) and the World Health Organization (WHO) revised glossary on ART terminology. Hum Reprod.2009:24:26832687.
3. Hoffman BL,Schorge JO,Schaffer JI et al. Williams Gynecology.2nd edition.Mc Graw Hill:2012.p.506-528
4. Inhorn M.C Global Infertility and the Globalization of New Reproductive Technologies: illustrations from Egypt.Soc.SciMed.2003:1837-51.
5. Jayanthi CR,divyashri M,sushma M.Adverse drug reaction in psychiatric outpatient clinical spectrum.J Cauality and Avoidability.
6. Agarwal Mukta, Das Vinita, Agarwal Anjoo et al. Assessment of Ovarian reserve in infertility. J Obstet Gynecol India,2009:59(6):569-572
7. Brunton LL, Chabner BA,Knollmann BC.Goodman and Gilman's The pharmacological Basis of Therapeutics.12th edition,Mc Graw Hill;2011.p.1163-1194.
8. Duru Shah,Sukhpreet Patel,Polycystic ovarian syndrome as a cause of recurrent pregnancy loss.J Obstet Gynecol India.2007057:5:p391-397.
9. Saghar Salehpour,Maryam Tamimi,Nasrin Sharkhiz.Comparison of oral dydrogesterone with suppository vaginal progesterone for luteal phase support in invitro fertilization (IVF): A randomized clinical trial.Iran J Reprod Med.2013.Nov:11(11):913-8.
10. Chuni Neena.Efficacy of sequential treatment of metformin and clomiphene citrate in clomiphene resistant women with polycystic ovarian syndrome. J Obstet Gynecol India 2007.57; 1: p69-72.